


CONCLUSION

If there exist any issues with the current amendment, Applicants respectfully request that an interview be granted with the undersigned attorney to discuss any remaining issues of problems with the foregoing amendment. The Examiner is invited to telephone the undersigned at (650) 496-1244 to arrange for a mutually convenient time and form for the interview.

Applicants believe that no fees are required; however, if any fees are required by the present Response, the Commissioner is authorized to charge any fees or credit any overpayment to DNAX Research Institute Deposit Account No. 04-1239.

Respectfully submitted,

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Sheela Mohan-Peterson  
Reg. No. 41,201

**Customer Number No. 028008**

DNAX Research Institute  
901 California Avenue  
Palo Alto, CA 94304-1104  
Tel: (650) 496-6400  
Fax: (650) 496-1200

VERSION WITH MARKINGS TO SHOW CHANGES

In the Specification:

Paragraph beginning at line 8 of page 4 has been amended as follows:

Figures 2A-[2C]2E show expression levels of hIL-7R $\alpha$  (Figures 2A-2B), R $\delta$ 2 (hTSLPR, Figures 2[B]C-2D), and IL-B50 in various tissues and cell types. Expression levels were normalized and expressed as femtograms mRNA per 50 ng total cDNA.

Paragraph beginning at line 26 of page 4 has been amended as follows:

Figures 6A-6C show[s] the surface phenotype of DC after treatment with medium alone, IL-B50, CD40-ligand (CD40L), IL-7 and LPS. IL-B50 is more potent than CD40-ligand and IL-7 in upregulating costimulatory molecules CD40 and CD80.

Paragraph beginning at line 18 of page 64 has been amended as follows:

In order to identify target cells capable of responding to IL-B50888888, a large panel of cDNA libraries was analyzed for the simultaneous expression of both hIL-7R $\alpha$  and hR $\delta$ 2, using quantitative PCR. Results of the expression analysis, conducted as described in materials and methods, are presented in Figures 2A-2[C]E. In particular, expression analysis of the two receptor subunits indicated that they were co-expressed primarily in activated dendritic cells, monocytes, and T cells (see, Figures 2A [and 2B] -2D) indicating that these cell types respond to human IL-B50. As shown in

Paragraph beginning at line 15 of page 65 has been amended as follows:

Additionally, the ability of IL-B50 to stimulate DCs to produce mRNAs for various cytokines and chemokines was compared with that of GM-CSF, IL-7, CD40-ligand (CD40L) and medium alone as a control, as follows. Purified CD11c+ DCs were cultured for 15-17 hours with IL-B50 (15 ng/ml), GM-CSF (100 ng/ml), IL-7 (50 ng/ml), CD40-ligand transfected L-cells (1 L-cell/4 DC) or medium alone. Total RNA was extracted and studied using real time quantitative PCR as described above. As shown in Figures 12A and 12C, IL-B50 did not stimulate human DCs to produce mRNA for [IL-1 $\alpha$ , IL-1 $\beta$ , IL-6, IL-12p40, TNF- $\alpha$ , MCP-1, MCP-4, Rantes and MIG, but did stimulate human DCs to produce mRNA for the chemokines TARC, MDC and [MIP3- $\beta$ ] MIP3- $\beta$  (Figure 12B).

Paragraph beginning at line 9 of page 67 has been amended as follows:

Freshly purified immature CD11c+ blood DC are known to spontaneously mature in culture. As shown in Figure 4A, loose and irregular clumps in the DC culture were evident after 24 hrs in medium alone. In the presence of IL-B50, this maturation process was dramatically enhanced. DC in culture formed tight and round clumps with fine dendrites visible at the periphery of each clump (Figure [6]4B). The IL-B50-induced maturation was confirmed by analyzing the surface phenotype of DC using flow cytometry. Whereas IL-B50 slightly upregulated the expression of HLA-DR and CD86, it strongly induced the costimulatory molecules CD40 and CD80 (Figure 5). This maturation process was accompanied by an increased viability of the DC. Additionally, IL-B50 was more potent than CD40-ligand (CD40L) and IL-7 in upregulating CD40 and

maximal at 15 ng/ml and above, and still significant at concentrations as low as 15 pg/ml.